

Derivation of R_0^T

The basic reproductive ratio, R_0 , is defined as the number of secondary infections from a single infected cell, assuming that virtually all cells are uninfected (i.e. $\dot{T} = \lambda - dT \Rightarrow T = \frac{\lambda}{d}$).

A simple derivation of R_0 from the basic model of HIV-1 in vivo dynamics is as follows:

$R_0 =$ target cell density \times burst size \times infection rate constant \times average lifetime of the virus

$$= \frac{\lambda}{d} \times n \times k \times \frac{1}{c}$$

For the crHIV-1 gene therapy model we defined a new R_0 for the crHIV-1 virus, R_0^T , defined as the number of secondary crHIV-1 infections obtained from a single crHIV-1 infection assuming that virtually all cells are uninfected by crHIV-1 but that the system is at steady state for HIV-1 infection (i.e. steady state for the basic model of HIV-1 in vivo dynamics:

$$\bar{T} = \frac{c}{kn}, \bar{V} = \frac{n\lambda}{c} - \frac{d}{k}, \bar{I} = \frac{\lambda}{\delta} - \frac{cd}{\delta kn}.$$

When $R_0^T \geq R_0$ crHIV-1 infection will persist, when $R_0^T < R_0$ crHIV-1 infection will die.

In order to derive the new R_0^T we segment the infection process into 2 components:

- 1) crHIV-1 infection of T cells
- and
- 2) HIV-1 infection of I_T cells.

The 1st component will yield roughly the density of I_T target cells for the 2nd component.

1)

target cell density for crHIV-1 \times crHIV-1 burst size \times crHIV-1 infectivity \times crHIV-1 lifetime

$$\left(\bar{T} = \frac{c}{kn}\right) \times P^2 Dn \times k \times \frac{1}{c}$$

$$= P^2 D\delta'$$

Essentially this is the λ value for the I_T cell population.

This is the I_T "target" cell density except that we have not accounted for the death rate of I_T cells (these cells die at a per cell rate of d). We now account for the average lifetime of I_T cells to find the actual target cell density:

$$\left(P^2 D\delta' \times \frac{1}{d}\right)$$

2)

I_T "target" cell density \times HIV-1 virus density \times HIV-1 infectivity

$$\begin{aligned} \left(P^2 D \delta' \times \frac{1}{d} \right) \times \bar{V} &= \frac{n\lambda}{c} - \frac{d}{k} \times k \\ &= P^2 D \left(\frac{n\lambda k}{dc} - 1 \right) \\ &= P^2 D (R_0 - 1) \quad [\zeta] \end{aligned}$$

But, in order, for crHIV-1 to persist we require $R_0^T \geq R_0$ or $\frac{R_0^T}{R_0} \geq 1$.

(This can be explained by considering the predator-prey model of 2 predator species competing for the same prey. Except in special cases, the principle of competitive exclusion applies, the species with the greater R_0 outcompetes or excludes the other predator species. Here, in our crHIV-1 model, if $R_0 > R_0^T$ then HIV-1 outcompetes crHIV-1 and excludes crHIV-1. But if the opposite is true $R_0^T > R_0$ then crHIV-1 is not excluded but will never outcompete or exclude HIV-1 since crHIV-1 replication depends on HIV-1).

Thus, we divide Eq. ζ above by R_0 and define R_0^T as:

$$R_0^T = P^2 D \left(1 - \frac{1}{R_0} \right)$$

When $R_0^T \geq 1$ crHIV-1 infection will persist in vivo, otherwise it will die out.

Below R_0^T was plotted relative to parameters P and D . The graph is cut-off at 1 on the z-axis, in order to emphasize the transition $R_0^T > 1$. The red and blue shading is added in order compare R_0^T to regimes where crHIV-1 is either unstable or stable. The red region corresponds to a regime where all eigenvalues of the Jacobian for Eqs.1-6 are negative for the solution to the Basic Model—thus only HIV-1 is stable (crHIV-1 is unstable and in fact a non-physical solution). The blue region corresponds to a regime where all eigenvalues of the Jacobian for Eqs.1-6 are negative for the solution to the expanded model—thus crHIV-1 is stable (the Basic Model solution is unstable). The purple spikes are a numerical anomaly and are irrelevant. The transcritical bifurcation (transition from red to blue) corresponds with $R_0^T = 1$. The regime where crHIV-1 is stable (blue) corresponds to regime $R_0^T > 1$.